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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,309	06/21/2001	Melissa K. Carpenter	090/002	9525

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EXAMINER	
FALK, ANNE MARIE	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,309	CARPENTER ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-47* is/are pending in the application.

4a) Of the above claim(s) *23-33 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed May 27, 2004 has been entered. Claims 34-38, 40, 44, 46, and 47 have been amended. Claim 48 has been cancelled.

Accordingly, Claims 23-47 remain pending in the instant application.

Claims 23-33 and 47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. Applicant timely traversed the restriction requirement in the reply filed on November 6, 2003.

Claims 34-46 are examined herein.

The objection to the specification is withdrawn in view of the amendment to the specification.

The rejections of Claims 34-46 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendments to the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description/New Matter

Claims 34-46 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants are referred to the final guidelines on written description published January 5, 2001 in the Federal Register at Volume 66, Number 4, pp. 1099-1111 (also available at www.uspto.gov).

The claims recite combinations without support in the original disclosure, thereby adding new matter to the claims.

The newly added claims recite **a system comprising two cell populations.** Claim 34 is directed to a system for producing differentiated cells from human embryonic stem (hES) cells, comprising:

a first cell population comprising undifferentiated hES cells; and

a second cell population comprising progeny of the hES cells in a medium containing one or more added TGF-β superfamily antagonists.

Claim 35 is directed to a system for producing differentiated cells from human embryonic stem (hES) cells, comprising:

a first cell population comprising undifferentiated hES cells; and

a second cell population, comprising at least ~10% hES-derived neural cells, identifiable by the criteria that they are progeny of said hES cells and express both MAP-2 and tyrosine hydroxylase. However, the new claims are not supported by the original disclosure because the original disclosure does not specifically contemplate this combination of two cell populations. At page 5 of the preliminary amendment (filed 11/6/03), Applicants refer to page 4, lines 34-35 of the specification as providing support for the new claims. The cited lines read "[t]his invention provides a system for efficient production of differentiated cells from primate pluripotent stem (pPS) cells." However, this section only provides support for certain elements of the claims and does not provide specific support for the combination of two cell populations now being claimed. The Examiner has carefully reviewed the entire specification and does not find support for the claimed invention as a whole. Applicants have not pointed to specific support for the new claims in the specification as-filed.

Thus, the amendment introduces new matter into the claims.

At pages 8-10 of the response, Applicants argue that the application demonstrates that Applicants were in possession of the claimed cell populations. Applicants appear to view the possession of the two cell populations by a single legal entity to be all that the claim requires. Applicants state that the two cell

populations do not have to be located in the same place at any given point in time (Declaration, section 7), nor would they necessarily be distributed together, although they could be (page 8 of the response, paragraph 3). The Declaration of Dr. Scott Thies has been fully considered but is not found to be persuasive. The Declaration asserts that someone who is using undifferentiated human ES cells in a protocol to produced differentiated neural cells bearing the markers recited in the claims would eventually be in possession of the system of two cell populations. The Declaration argues that "[i]t would not be necessary for the user to have possession of the two cell populations at the same time, since a population of undifferentiated hES cells could be caused to differentiate to neural cells in its entirety." The Declarant further argues that a scientist knowledgeable in this area would understand the benefit of retaining some of the ES cells in the undifferentiated state, since the undifferentiated cells can be further expanded to produce differentiated cells. The Declarant states that "[t]o this day, Geron Corporation continues to maintain hES cell lines in both the undifferentiated form [*sic*], producing neural cells whenever needed in the quantity required." By this argument it would appear that Geron Corporation is the claimed system that comprises the two separate cell populations. However, patent claims directed to legal entities are not patentable subject matter within the context of 35 U.S.C. 101. The Examiner agrees that Applicants were in possession of each separate cell population recited in the claims and therefore claims directed to either cell population would not be rejected for lack of written description, although they would likely be subject to other rejections. However, the **combination** of the two cell populations is not described in the specification and therefore constitutes new matter, for lack of written description.

Enablement

Claims 34-46 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, are set forth in *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988). These factors include: (1) the nature of the invention, (2) the state of the prior art, (3) the relative level of skill of those in the art, (4) the predictability of the art, (5) the breadth of the claims, (6) the amount of direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary.

The following factors have been considered.

Nature of the invention. The claims are directed to a system comprising two cell populations. As claimed, the two cell populations are intended to be used together somehow. However, the specification does not specifically disclose how to use these two cell populations together. The specification contemplates that the cells of the invention can be used in drug screening. However, the specification does not disclose how one would use the claimed **system of two cell populations** in drug screening. The specification also discloses that the cell populations are intended to be used for therapeutic transplantation (see the specification at page 24, lines 20-22). The specification states that "[c]ells prepared according to this invention that are useful for human or veterinary therapy are optimally supplied in a pharmaceutical composition ..." (page 25, lines 5-6). The specification contemplates using a variety of differentiated cell types, such as neural cells, cardiomyocytes, and hepatocytes, for therapeutic transplantation (page 24, lines 19-41). However, the specification does not address how to use the **system of two** cell populations. As discussed above, the specification does not specifically contemplate a **system of two** cell populations as claimed.

Amount of direction or guidance presented and the presence or absence of working examples. The specification discloses in Example 5 the testing of various factors for use in the differentiation of hES cells to neurons. However, none of the examples demonstrate the use of the claimed **system of two cell populations.** As discussed above, the specification does not contemplate a **system of two** cell populations as claimed. Thus, the specification does not adequately teach how to use

the claimed compositions. Furthermore, none of the examples demonstrate a therapeutic use of the system of two cell populations.

The specification contemplates using the various "differentiated cells of this invention" to screen candidate compounds or environmental conditions that affect differentiation or metabolism of a cell type of interest" (page 5, lines 36-37). Again however, the specification does not provide any guidance for using the claimed **system of two** cell populations in drug screening assays. The specification must provide specific guidance for the use of the **claimed** compositions. Here it does not.

It is not to be left up to the skilled artisan to figure out how to use the claimed compositions. The courts held that the disclosure of an application shall inform those skilled in the art how to use applicant's claimed invention, not how to **find out** how to use it for themselves. *In re Gardner et al.* 166 USPQ 138 (CCPA 1970). With regard to the differentiated cells described in the specification, this specification only teaches what is intended to be done and how it is intended to work, but does not actually teach how to do that which is intended. With regard to the **claimed** compositions, the specification does not provide any guidance for their use.

State of the prior art and predictability of the art. The state of the art is such that very little is known about the cell types that can be used to restore neurological function. One of the lingering questions in the field of stem cell research relates to the stage of differentiation of stem cells useful for transplantation and whether the same stage will be useful for all transplantation applications, or vary on a case-by-case basis (see p. ES-8, column 1 of Stem Cells: Scientific Progress and Future Research Directions, June 2001).

In a review of the state of the art of stem cell technology, the National Institutes of Health acknowledge the potential usefulness of stem cells in theraeutic transplantation and the possible development of therapeutic protocols in the future (see Stem Cells: Scientific Progress and Future Research Directions, June 2001). However, the review also illustrates that there are numerous and significant obstacles that must be overcome. As such, the asserted utility of the present invention,

directed to using the claimed compositions in therapeutic transplantation constitutes a credible utility, albeit one that is not enabled by the instant specification. The instant rejection therefore is not for lack of utility, but rather for lack of enablement for the asserted utility. Furthermore, the asserted utilities of therapeutic transplantation or drug screening are the only utilities disclosed for the differentiated cells referred to in the specification. However, the specification does not provide specific guidance for the use of the **claimed** compositions (the system of two cell populations). With regard to therapeutic transplantation, there is no teaching at all for using the claimed combinations of cell populations in therapeutic transplantation. With regard to drug screening, there is no teaching at all for using the claimed combinations of cell populations in drug screening assays. For the reasons discussed herein, the specification does not teach how to use the **claimed** compositions for the utilities contemplated for the **differentiated cells** referred to in the specification.

The specification fails to provide an enabling disclosure for using the claimed compositions in accordance with the utilities asserted in the specification for differentiated cells (*i.e.*, for drug screening or therapeutic transplantation). The utilities asserted in the specification are directed to uses for precursor cells and terminally differentiated cells, but not to the specific combination of cell populations instantly claimed.

The specification fails to provide an enabling disclosure for using the claimed compositions to provide a therapeutic benefit because the specification does not provide **specific guidance** regarding how to use the claimed compositions therapeutically. In unpredictable arts, it is the specification itself that must provide the novel teachings for using the claimed compositions therapeutically. The specification does not offer any guidance as to how the claimed compositions could be used therapeutically for the treatment of any disorder. No working examples demonstrate a therapeutic effect in a diseased animal upon transplantation of the claimed compositions. The specification contemplates that "cells of the invention" can be used therapeutically. Accordingly, the specification must teach how to use the claimed compositions in transplantation protocols to produce a therapeutic effect. However, the specification does

not teach how to produce a therapeutic effect in any animal. The specification fails to provide any guidance relating to the amount of cells to inject, the site of injection, and extent of cellular persistence required to provide any therapeutic benefit for any disorder. There are no teachings regarding the administration of the two separate cell populations recited in the claims. There is no guidance relating to the order of administration of the two cell populations, the physical location for implantation of each cell population, or the route of administration for the two cell populations, whether the same or different.

The court has recognized that physiological activity is unpredictable. *In re Fisher*, 166 USPQ 18 (CCPA 1970). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved. *In re Fisher*, 166 USPQ 18 (CCPA 1970).

Given the limited working examples, the limited guidance provided in the specification, the lack of any showing of therapeutic benefit upon transplantation of the claimed compositions, the lack of any use for the claimed compositions in drug screening assays, the broad scope of the claims, and the unpredictability for producing a therapeutic effect upon transplantation of the claimed compositions (consisting of a system of two cell populations), undue experimentation would have been required for one skilled in the art to use the claimed compositions in methods of transplantation to produce a therapeutic effect or in drug screening assays.

At pages 11-12 of the response, Applicants argue that product claims need only be enabled for *one* of the possible uses of the invention in order to comply with the enablement requirement. Applicants further argue that the neural cells can be used in drug screening and that a lengthy discussion of drug screening using the neural cells of this invention is described in the section beginning on page 21. As discussed above, the Examiner agrees that the neural cell populations are useful for drug screening, but such a use is directed to the second cell population, not the **combination** of the two cell populations.

Applicants further argue that hES derived neural cells can be used therapeutically, but again this argument refers to a use for the second cell population rather than the combination of the two cell

populations. Since the specification fails to disclose an enabled use for the combination, the rejection under 35 U.S.C. 112, first paragraph, for lack of an enabling disclosure is maintained for reasons of record.

Conclusion

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history

information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 10:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (571) 272-0804. The central official fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER